

## REMARKS

Upon entry of the foregoing amendments, claims 1, 3-8, 11-16, 18-21 and 23-29 will be pending in the present patent application. Claims 26 to 29 are withdrawn from consideration subject a Restriction Requirement. Claims 1, 3-8 and 11-25 are rejected. In view of the foregoing amendments and the following remarks, reconsideration and withdrawal of the present basis for rejecting the claims herein of this application are respectfully requested.

### **I. Discussion of the Amendment**

Claim 1 is amended to delete the term " $Z^2$ -(lower alkyl)" in the definition of  $R^4$ , and the terms " $C(=O)-CH_2OH$ " and " $C(=O)-CH_2SH$ " in the list of acid bioisosteres.

Claims 3, 4 and 23 are amended to be dependent upon claim 1.

Claim 14 is amended to delete the phrase "optionally substituted phenyl or optionally substituted heteroaryl is".

Claim 20 is amended to delete the phrases "azaheterocyclyl, azaheterocyclenyl, or heteroaryl" and "at least", and to replace the term "may be" with "is" in the definition of  $Z^1$ .

Claim 21 is amended to delete the phrase "at least".

Claim 23 is also amended to delete the phrase "optionally substituted fused arylcycloalkyl, optionally substituted fused arylcycloalkyl, optionally substituted fused arylcycloalkenyl, optionally substituted fused arylheteroaryl, optionally substituted fused heteroarylaryl, optionally substituted fused heteroaryl-cycloalkyl, optionally substituted fused heteroaryl-cycloalkenyl, optionally substituted fused heteroaryl-heterocyclyl, optionally substituted fused heteroaryl-heterocyclenyl" in the definition of  $R^2$ , and to reflect more proper Markush claim format.

Claim 24 is amended to delete the second occurrence of the species "2-[1-Biphenyl-4-carbonyl]-pyrrolidin-2-yl]-3-(3-carbamimidoylphenyl)-propionic acid methyl ester trifluoroacetate", to add the missing half parenthesis "(" in the eighth species, to delete the species "2-[1-(Biphenyl-4-carbonyl)-pyrrolidin-2-yl]-3-(1H-pyrrolo[3,2-c]pyridin-2-yl)-propionic acid methyl ester trifluoroacetate", "2-[1-(Biphenyl-4-carbonyl)-D-pyrrolidin-2-yl]-3-(1H-pyrrolo[2,3-c]pyridin-2-yl)-propionic acid methyl ester-trifluoroacetate", "3-(4-Amino-quinazolin-6-yl)-2-[1-(biphenyl-4-carbonyl)-D-pyrrolidin-2-yl]-propionic acid methyl ester-ditrifluoroacetate", and "3-(R)-(3-Carbamimidoylphenyl)-2-(R)-[1-[4-(6-oxo-16-dihydropyrid-3-yl)-benzoyl]-pyrrolidin-2-yl]-propionic acid methyl ester trifluoroacetate", to reflect more proper Markush claim format, and to correct a grammatical error.

Claims 7 and 22 are cancelled, without prejudice.

Applicants reserve the right to pursue the cancelled subject matter of claims in a subsequent application.

Applicants submit that this amendment does not add any new matter.

## II. Discussion of the Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 1, 3-8 and 11-25 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly "being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention" (Action at page 3). Specifically, the Examiner alleges that:

a) Claims 1, 3-8, 11-23 and 25 are vague and indefinite in that it is not known what is meant by the variable  $Z^2$  within the definition of  $R^4$  where  $Z^2$  is not defined within the claim 1.

Applicants submit that claim 1 has been amended to delete the term " $Z^2$ -(lower alkyl)" in the definition of  $R^4$ . Such amendment obviates the instant rejection on claims 1, 3-8, 11-23 and 25.

b) Claims 1, 3-8, 11-23 and 25 are vague and indefinite in that it is not known what is meant by the  $C(=O)-CH_2OH$  and  $C(=O)-CH_2SH$  moieties in the list of acid bioisosteres in claim 1.

Applicants submit that claim 1 has been amended to delete the terms " $C(=O)-CH_2OH$ " and " $C(=O)-CH_2SH$ " in the list of acid bioisosteres. Such amendment obviates the instant rejection on claims 1, 3-8, 11-23 and 25.

c) Claims 3, 4 and 23 are vague and indefinite in that it is not known what is meant by the claim dependency where these claims are dependent on a cancelled claim.

Applicants submit that claims 3, 4 and 23 have amended to be dependent upon claim 1. Such amendment obviates the instant rejection on claims 3, 4 and 23.

d) Claim 14 is vague and indefinite in that it is not known what is meant by the definition of  $R^2$  where  $R^2$  is optionally substituted phenyl or optionally substituted heteroaryl is optionally...

Applicants submit that claim 14 has been amended to delete the phrase "optionally substituted phenyl or optionally substituted heteroaryl is". Such amendment obviates the instant rejection on claim 14.

e) Claim 17 recites the limitation "hydrogen" in the definition of  $R^5$  and  $R^6$ . There is insufficient antecedent basis for this limitation in the claim.

Applicants submit that cancellation of claim 17, without prejudice, obviates the instant rejection on claim 17.

f) Claim 20 recites the limitation "azaheterocyclyl, azaheterocyclenyl, or heteroaryl" in the definition of Z<sup>1</sup>. There is insufficient antecedent basis for this limitation in the claim.

Applicants submit that claim 20 has been amended to delete the phrases "azaheterocyclyl, azaheterocyclenyl, or heteroaryl" in the definition of Z<sup>1</sup>. Such amendment obviates the instant rejection on claim 20.

g) Claim 20 recites the limitation "which **may be** substituted by an amidino substituent" in the definition of Z<sup>1</sup>. There is insufficient antecedent basis for this limitation in the claim.

Applicants submit that claim 20 has been amended to replace the term "may be" with "is" in the definition of Z<sup>1</sup>. Such amendment has sufficient antecedent basis in claim 1, thus, obviates the instant rejection on claim 20.

h) Claim 20 recites the limitation "at least" in the definition of Z<sup>1</sup>. There is insufficient antecedent basis for this limitation in the claim.

Applicants submit that claim 20 has been amended to delete the phrases "at least" in the definition of Z<sup>1</sup>. Such amendment obviates the instant rejection on claim 20.

i) Claim 21 recites the limitation "at least" in the definition of Z<sup>1</sup>. There is insufficient antecedent basis for this limitation in the claim.

Applicants submit that claim 21 has been amended to delete the phrases "at least" in the definition of Z<sup>1</sup>. Such amendment obviates the instant rejection on claim 21.

j) Claim 22 recites the limitation "optionally substituted azaheteroaryl, optionally substituted azaheterocyclyl, optionally substituted azaheterocyclenyl, optionally substituted fused arylazaheteroaryl, optionally substituted fused azaheteroarylaryl, optionally substituted fused azaheteroarylcycloalkyl, optionally substituted fused azaheteroarylcycloalkenyl, optionally substituted fused azaheteroarylheterocyclyl, optionally substituted fused azaheteroarylheterocyclenyl, optionally substituted fused azaheteroarylazaheterocyclyl, optionally substituted fused azaheteroarylazaheterocyclenyl group" in the definition of Z<sup>1</sup>. There is insufficient antecedent basis for this limitation in the claim.

Applicants submit that cancellation of claim 22, without prejudice, obviates the instant rejection on claim 22.

k) Claim 23 is vague and indefinite in that it is not known what is meant by the second occurrence of optionally substituted fused arylcycloalkyl in the definition.

l) Claim 23 recites the limitation "optionally substituted fused arylcycloalkyl, optionally substituted fused arylcycloalkyl, optionally substituted fused arylcycloalkenyl, optionally substituted fused arylheteroaryl, optionally substituted fused heteroarylaryl, optionally substituted fused heteroarylcyloalkyl, optionally substituted fused heteroarylcyloalkenyl, optionally substituted fused heteroarylheterocyclyl, optionally substituted fused heteroarylheterocyclenyl" in the definition of  $R^2$ . There is insufficient antecedent basis for this limitation in the claim.

Applicants submit that claim 23 has been amended to delete the phrase "optionally substituted fused arylcycloalkyl, optionally substituted fused arylcycloalkyl, optionally substituted fused arylcycloalkenyl, optionally substituted fused arylheteroaryl, optionally substituted fused heteroarylaryl, optionally substituted fused heteroarylcyloalkyl, optionally substituted fused heteroarylcyloalkenyl, optionally substituted fused heteroarylheterocyclyl, optionally substituted fused heteroarylheterocyclenyl" in the definition of  $R^2$ . Such amendment obviates the above rejections k) and l) on claim 23.

m) Claim 24 is vague and indefinite in that it is not known what is meant by the second occurrence of the species 2-[1-Biphenyl-4-carbonyl)-pyrrolidin-2-yl]-3-(3-carbamimidoylphenyl)-propionic acid methyl ester trifluoroacetate, i.e., the first and seventh species.

Applicants submit that claim 24 has been amended to delete the second occurrence of the species "2-[1-Biphenyl-4-carbonyl)-pyrrolidin-2-yl]-3-(3-carbamimidoylphenyl)-propionic acid methyl ester trifluoroacetate", i.e., the seventh species. Such amendment obviates the instant rejection on claim 24.

n) Claim 24 is vague and indefinite in that it is not known what is meant by the nomenclature of the species 2-[1-Biphenyl-4-carbonyl)-pyrrolidin-2-yl]-3-(3-carbamimidoylphenyl)-propionic acid methyl ester trifluoroacetate and 2-[1-Biphenyl-4-carbonyl)-pyrrolidin-2-yl]-3-(4-carbamimidoylphenyl)-propionic acid methyl ester trifluoroacetate, i.e., the seventh and eighth species.

Applicants submit that claim 24 has been amended to delete the seven species 2-[1-Biphenyl-4-carbonyl)-pyrrolidin-2-yl]-3-(3-carbamimidoylphenyl)-propionic acid methyl ester trifluoroacetate, and to add the missing half parenthesis "(" in the eighth species so that the eighth species now reads as 2-[1-(Biphenyl-4-carbonyl)-pyrrolidin-2-yl]-3-(4-carbamimidoylphenyl)-propionic acid methyl ester trifluoroacetate instead of 2-[1-Biphenyl-4-carbonyl)-pyrrolidin-2-yl]-3-(4-carbamimidoylphenyl)-propionic acid methyl ester trifluoroacetate. Such amendment obviates the instant rejection on claim 24.

o) Claim 24 recites the limitation "1H-pyrrolo[3,2-c]pyridine-2-yl" in the nomenclature of the ninth species. There is insufficient antecedent basis for this limitation in the claim.

Applicants submit that claim 24 has been amended to delete the ninth species, i.e., 2-[1-(Biphenyl-4-carbonyl)-pyrrolidin-2-yl]-3-(1H-pyrrolo[3,2-c]pyridin-2-yl)-propionic acid methyl ester trifluoroacetate. Such amendment obviates the instant rejection on claim 24.

p) Claim 24 recites the limitation "1H-pyrrolo[3,2-c]pyridine-2-yl" in the nomenclature of the tenth species. There is insufficient antecedent basis for this limitation in the claim.

Applicants submit that claim 24 has been amended to delete the tenth species, i.e., 2-[1-(Biphenyl-4-carbonyl)-D-pyrrolidin-2-yl]-3-(1H-pyrrolo[2,3-c]pyridin-2-yl)-propionic acid methyl ester-trifluoroacetate. Such amendment obviates the instant rejection on claim 24.

q) Claim 24 recites the limitation "4-amino-quinazolin-6-yl" in the nomenclature of the eleventh species. There is insufficient antecedent basis for this limitation in the claim.

Applicants submit that claim 24 has been amended to delete the eleventh species, i.e., 3-(4-Amino-quinazolin-6-yl)-2-[1-(biphenyl-4-carbonyl)-D-pyrrolidin-2-yl]-propionic acid methyl ester-ditrifluoroacetate. Such amendment obviates the instant rejection on claim 24.

r) Claim 24 is vague and indefinite in that it is not known what is meant by 6-oxo-16-dihydropyrid-3-yl in nomenclature of the twelfth species.

Applicants submit that claim 24 has been amended to delete the twelfth species, i.e., 3-(R)-(3-Carbamimidoylphenyl)-2-(R)-[1-[4-(6-oxo-16-dihydropyrid-3-yl)-benzoyl]-pyrrolidin-2-yl]-propionic acid methyl ester trifluoroacetate. Such amendment obviates the instant rejection on claim 24.

s) Claim 24 is vague and indefinite in that it is not known what is meant by the "or" which appears before the fifteen species indicating the end of the Markush Group which is not so.


Applicants submit that claim 24 has been amended to delete the "or" that appears before the fifteen species to reflect more proper Markush claim format. Such amendment obviates the instant rejection on claim 24.

In view of the forgoing amendment and remarks, Applicants respectfully request reconsideration and withdrawal of the instant rejections on claims 1, 3-8 and 11-25.

III. Conclusion

Applicants respectfully submit that this application is now in condition for allowance. Accordingly, an indication of allowability and an early Notice of Allowance are respectfully requested. If there are any issues that can be resolved by a telephone conference or an Examiner's amendment, the Examiner is invited to call the undersigned attorney at (908) 231-3582.

Respectfully submitted,



Dated: March 14, 2007

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